A gene regulatory network subcircuit drives a dynamic pattern of gene expression.

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Public Summary:
Both stem cell differentiation and tissue regeneration are highly dynamic processes involving the sequential transcription (or "activation") of specific genes. To uncover how to predictively manipulate these multi-step processes for therapeutic purposes, we must understand how these events occur over time. However, dynamic processes are difficult to study in (asynchronous) cultures of stem cells or in the multi-step (often multi-day or week) processes of tissue regeneration. We take advantage of a system, the developing sea urchin embryo, that allows us to understand complex, multi-gene and, importantly, dynamic activation of specific genes. This system allows us to use advanced methods of functional genomics to capture both a comprehensive view of gene regulation and a detailed, mechanistic understanding of gene regulation over time. We determined the mechanisms controlling how initial patterns of gene expression are formed, a process directly related to initial stem cell differentiation. We found a small set of interactions drive this process. These interactions use and then re-use the same regulatory elements encoded in the genomes and thus the "static" genomic sequences encode a dynamic process.

Scientific Abstract:
Early specification of endomesodermal territories in the sea urchin embryo depends on a moving torus of regulatory gene expression. We show how this dynamic patterning function is encoded in a gene regulatory network (GRN) subcircuit that includes the otx, wnt8, and blimp1 genes, the cis-regulatory control systems of which have all been experimentally defined. A cis-regulatory reconstruction experiment revealed that blimp1 autorepression accounts for progressive extinction of expression in the center of the torus, whereas its outward expansion follows reception of the Wnt8 ligand by adjacent cells. GRN circuitry thus controls not only static spatial assignment in development but also dynamic regulatory patterning.